Hepatitis C Virus (HCV) Epidemiology in the United States: Emerging Trends

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Presenter Disclosures

Scott Holmberg, MD, MPH

(1) The following personal financial relationships with commercial interests relevant to this presentation existed during the past 12 months:

No relationships to disclose

A Tale of Two Epidemics

- Chronic HCV: Rapidly increasing mortality and morbidity

- Acute HCV: The “emerging” epidemic of new HCV infections in young persons who inject drugs (PWIDs)

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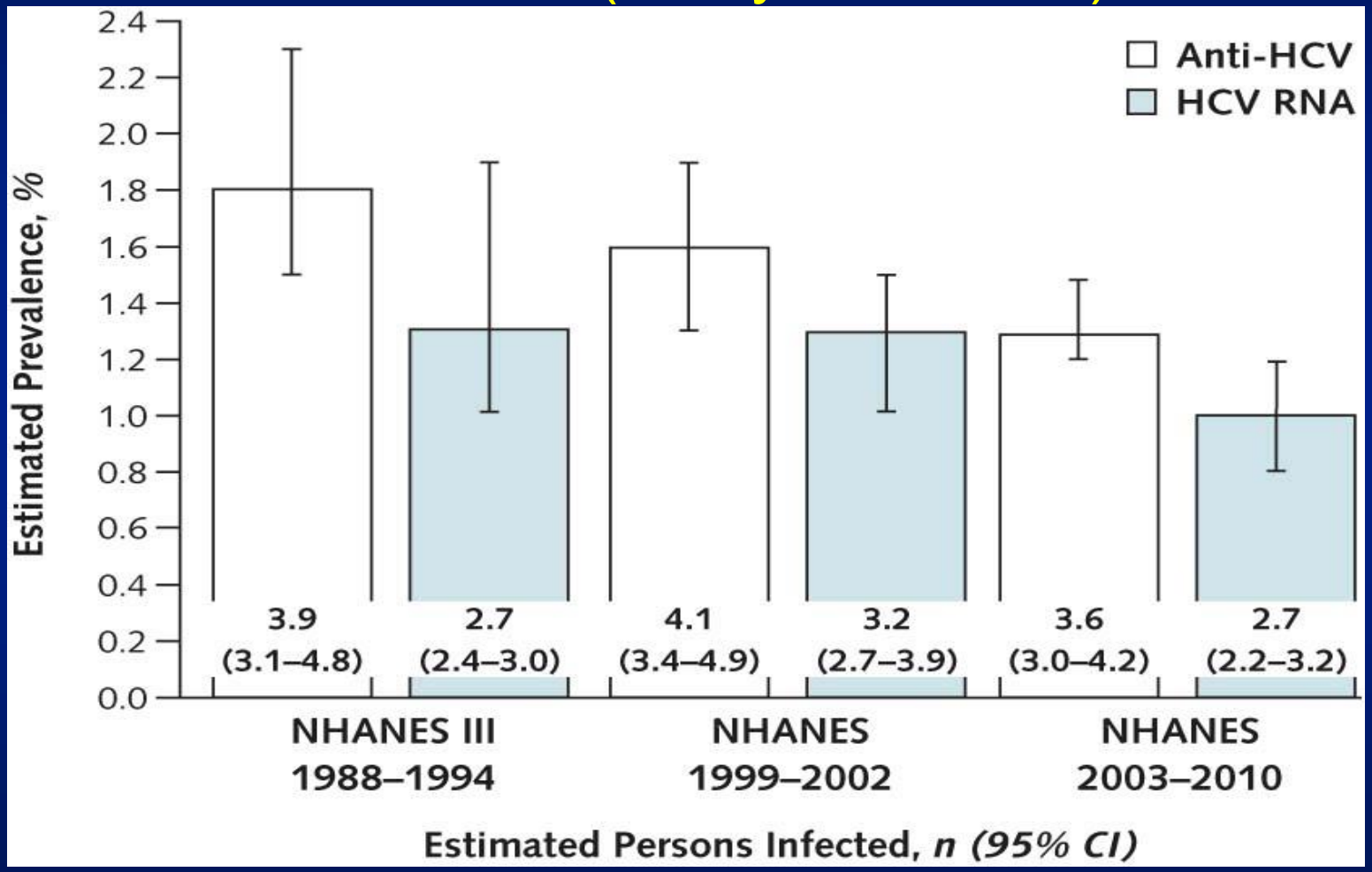
Somewhat declining prevalence, but still 3.2m HCV-infected US residents, 75% born between 1945-1965 ('Baby Boomers")



From: MM Denniston et al *Ann Intern Med* 2014; 160:293-300

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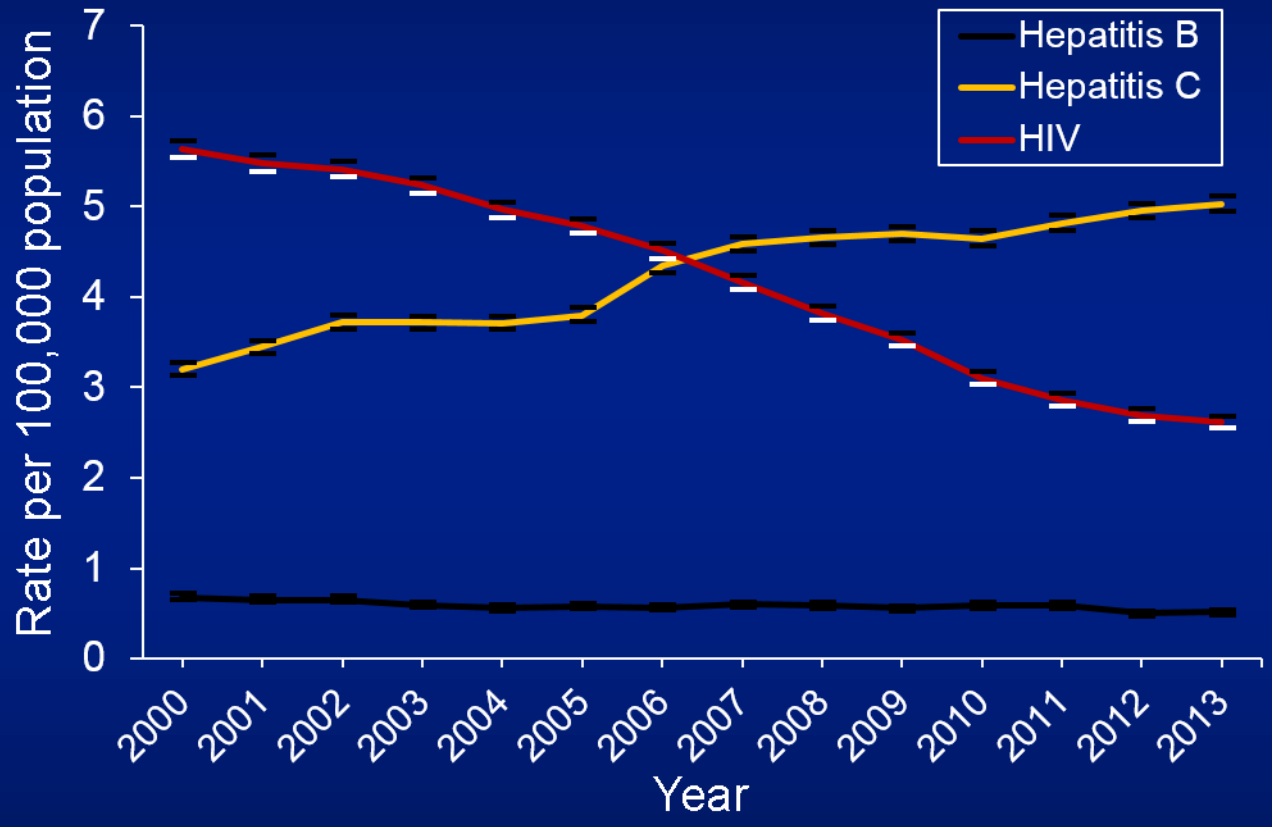
Annual age-adjusted mortality rates from hepatitis B and hepatitis C virus and HIV infections listed as causes of death in the United States between 2000-2013



Extended from: KN Ly et al, *Ann Intern Med* 2012; 156:271-8.

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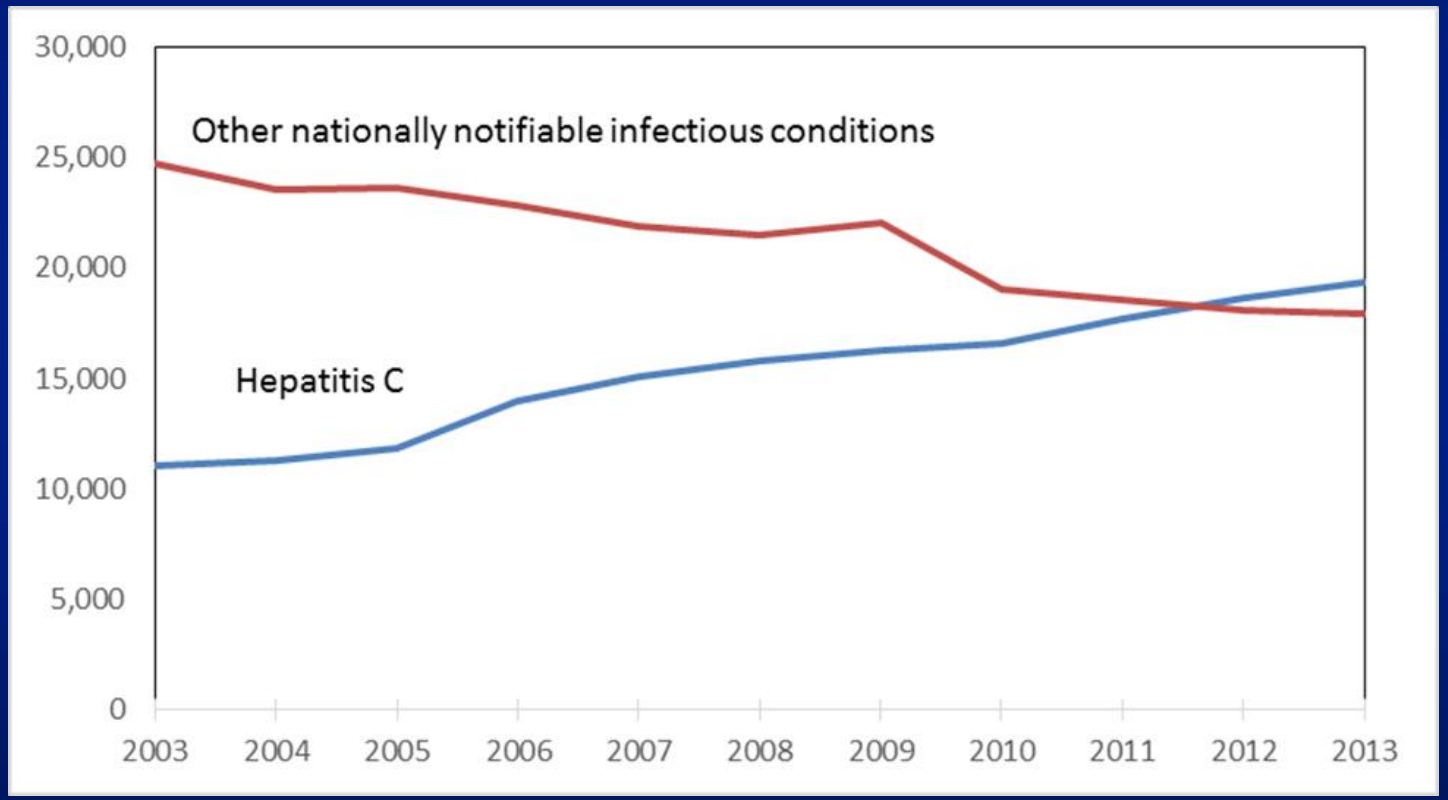
And this continues to increase “under the radar”

Figure. Annual number of deaths from hepatitis C virus and all other 60 nationally notifiable infectious conditions* listed as multiple causes of death in the United States between 2003 and 2013.



* 61 infectious conditions, as reported to CDC

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Hidden Mortality From HCV is Increasing:
Data from the Chronic Hepatitis Cohort Study (CHeCS)*

- 1600 deaths in well-characterized HCV patients, 2006- 2010
- Mean age at death – 59 years
- Under counted by vital records: Only 19% of HCV patients who died had HCV noted anywhere on their death certificates….and this was despite that >75% had pre-mortem evidence of liver disease
- Implies > 100 000 deaths/yr–- >75 000 attributable to HCV–- in HCV-infected persons in US

**From*: R Mahajan et al, *Clin Infect* Dis 2014; 58:1055-61.

The new all-oral medicines for HCV

- One pill/day for 12 weeks cures >95% people
- However, a pill originally cost $1,000 each, thus over $84,000 for a complete course
- While total treatment costs have now been negotiated by most insurers < $50,000 for a complete course—which, incidentally, is what previous less effective therapies cost-- this still is a staggering cost burden given the many HCV patients

AASLD/IDSA/IAS-USA Guidelines 2015

“Highest Priority” for Treatment (High risk for mortality/morbidity)

- Advanced fibrosis (Metavir F3) or compensated cirrhosis (F4)
- Organ transplant
- Type 2 or 3 essential mixed cryoglobulinemia with end-organ manifestations (eg, vasculitis)
- Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis

“High Priority” for Treatment (High Risk for Complications)

- Fibrosis (Metavir F2)
- HIV-1 coinfection
- Hepatitis B virus (HBV) coinfection
- Other coexistent liver disease (eg, [NASH])
- Debilitating fatigue
- Type 2 Diabetes mellitus (insulin resistant)
- Porphyria cutanea tarda

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So, in 2015, we are kind of “stuck”

- One side: treatment even at $ 84k per patient is cost-effective
- Other side: we do not have funds to treat 3.2 million at this drug cost
- However:
  - We all agree to treat sickest first
  - Drug prices have come down
  - Cost-effectiveness analysis indicates if we can get prices below $30,000 it would make sense to treat everyone

Calculating Numbers at "Highest" and "High" Priority for Treatment

U.S. household population with chronic HCV infection
2.7 million*

↓

HCV diagnosed (50%)
1.35 million**

↓

Staged by biopsy or laboratory data available to calculate a FIB-4 score (94%)
1.27 million

Biopsy (22%):	**297,000**
FIB-4 score* only (72%):**	**972,000**

↓

Meet AASLD/IDSA/IAS-US "highest priority" or "high priority" treatment criteria (64%)
813,000

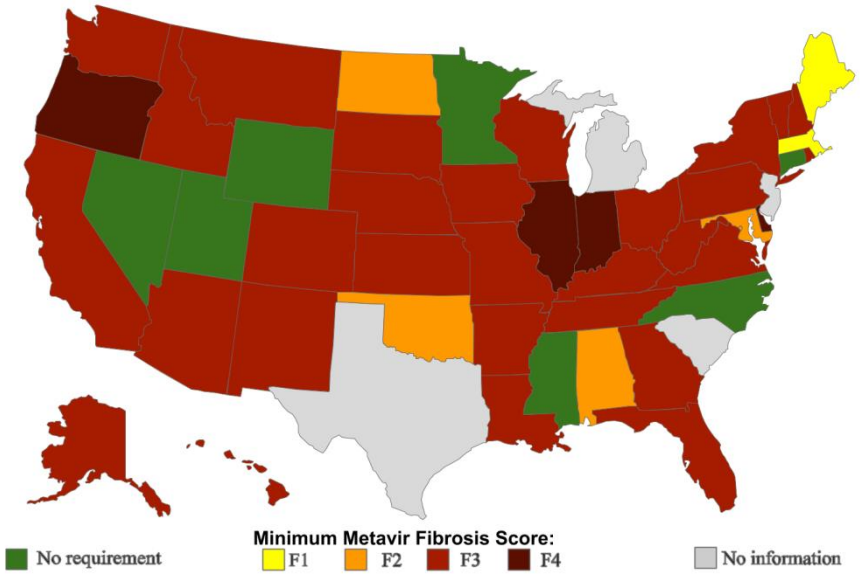
Highest priority		**457,000**
Metavir F3 or higher (33%):	**419,000**	
Lower than F3 with kidney disease (3%):	**38,000**	
High priority		**356,000**
Metavir F2 (22%):	**280,000**	
Less than F2 with chronic condition (6%):	**76,000**	

From: Xu et al, *Am J Publ He*alth 2015 Jul;105(7):1285-9

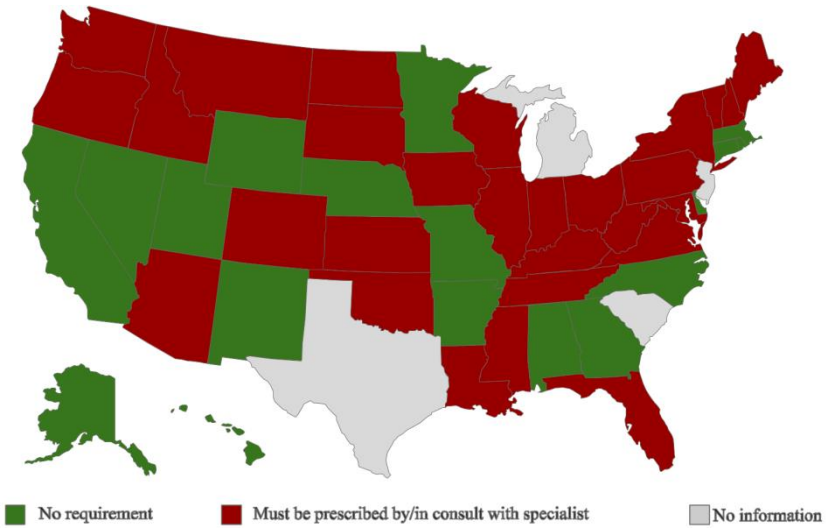
*MM Denniston, et al. *Ann Intern Med*, 2014; 160: 293-301; **SD Holmberg, et al. *N Engl Med* 2013; 368: 1859-1861; ***SD Holmberg et al. *Clin Inf Dis*, 2013; 57: 240-6.
FIB-4 score =[age x AST (IU L^{-1})]/[platelet (10^3 μL^{-1}) x ALT½ (IU L^{-1})]; FIB-4 score $\geq$ 2.5 is predictive of advanced fibrosis Metavir F3 or higher, while a FIB-4 score $\geq$ 1.6 but less than 2.5 is predictive of advanced fibrosis Metavir F2.

State Medicaid Restrictions

- **Minimum fibrosis score**

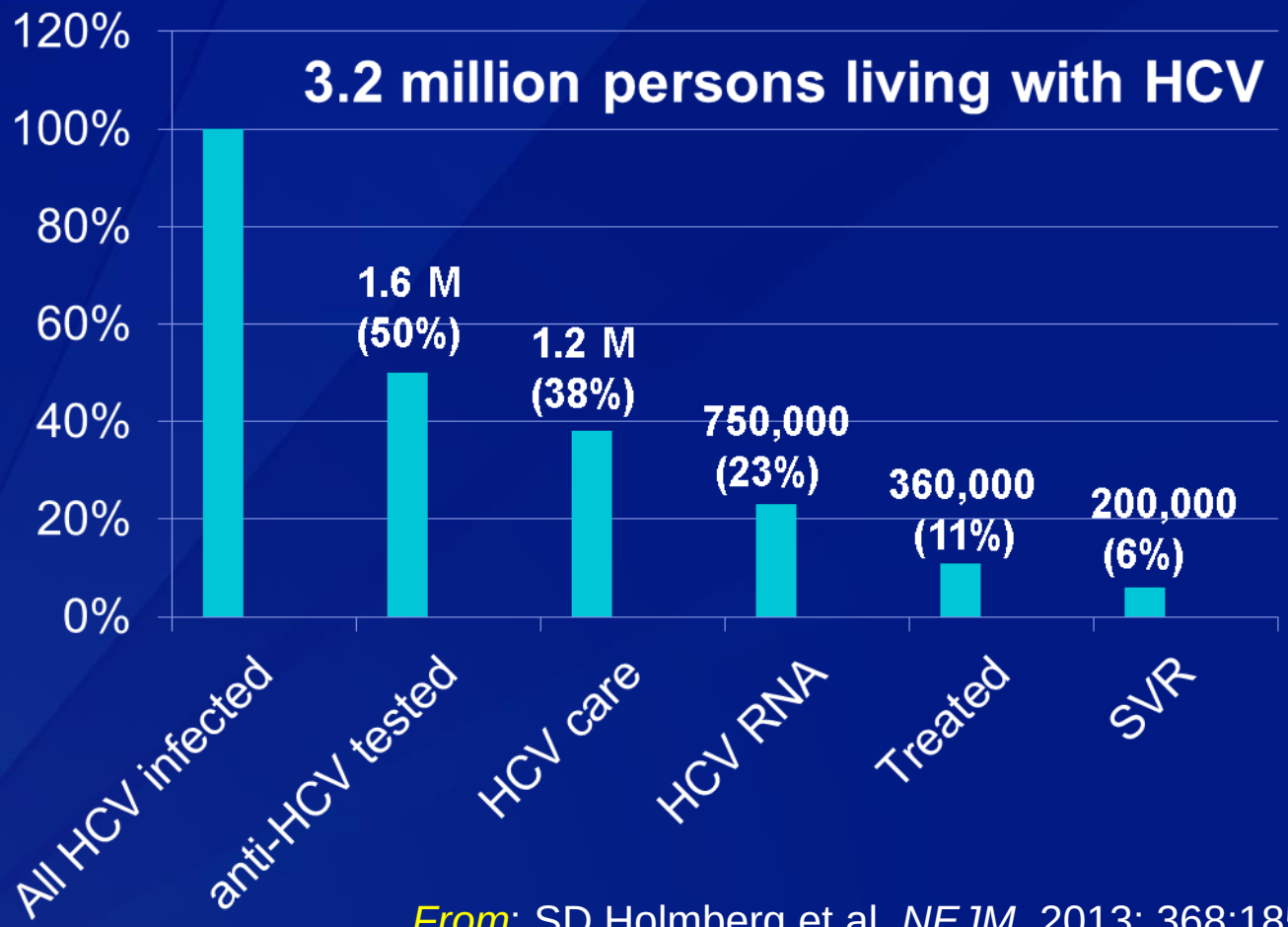


- **Prescription by specialist**



Frequent barriers to treatment: No alcohol or drugs in previous 6 months. Some states require biopsies for fibrosis scoring or finding a 'Fibroscan' machine to document liver fibrosis/cirrhosis: this is often a barrier. For those in more rural areas, finding a specialist, as required by many state Medicaid offices, can be very difficult.

Improving the HCV Test and Cure Continuum: current efforts to intervene at each of these steps



From: SD Holmberg et al, *NEJM* 2013; 368:1859-62, based on data from CHeCS and NHANES

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The Second "Emerging" Epidemic….

- Increasing HCV in young persons…in places we didn't expect…

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Figure 4.1. Reported number of acute hepatitis C cases — United States, 2000–2013

Source: National Notifiable Diseases Surveillance System (NNDSS)

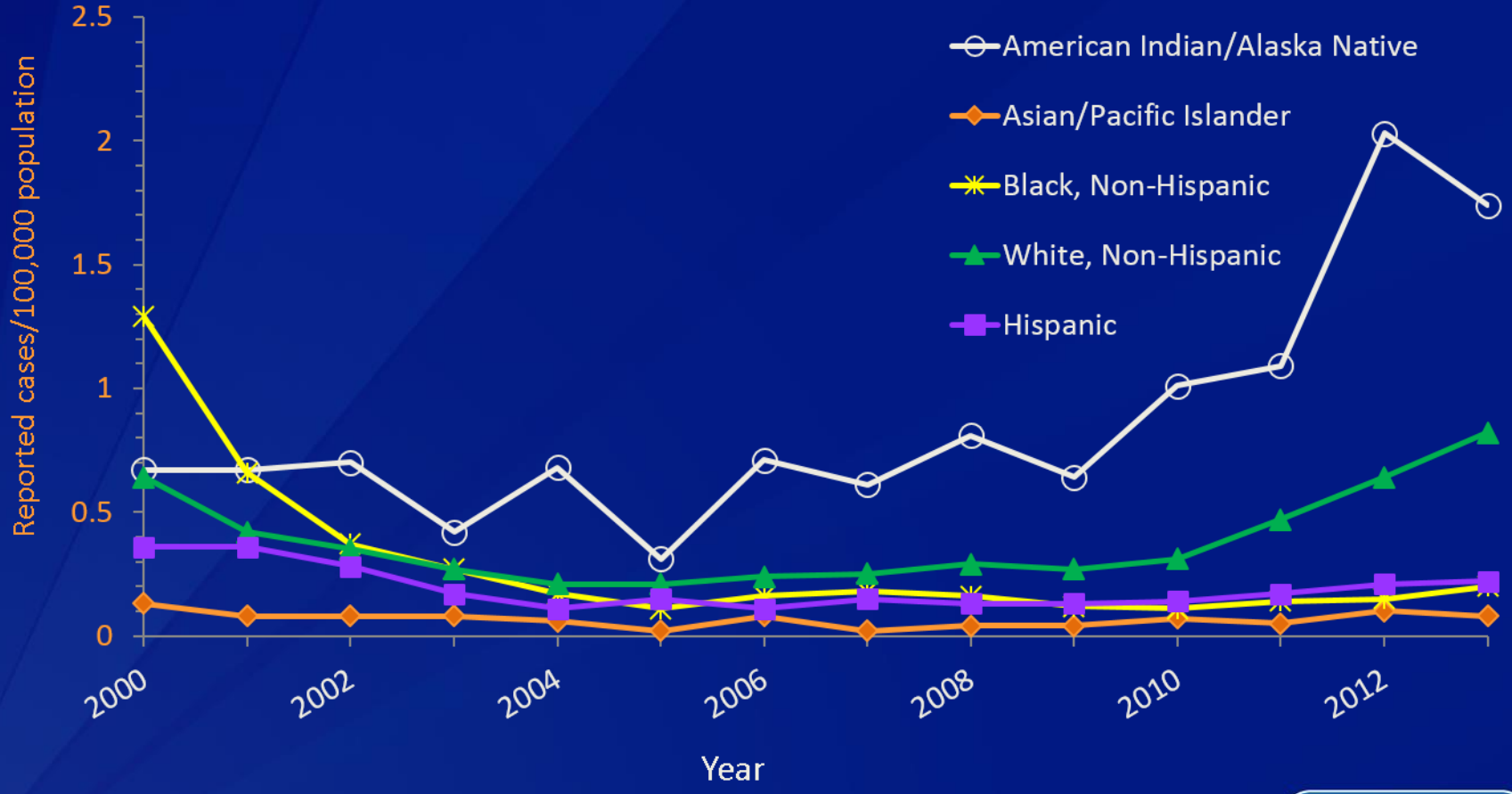
Figure 4.2. Incidence of acute hepatitis C, by age group — United States, 2000–2013

Source: National Notifiable Diseases Surveillance System (NNDSS)

Figure 4.3. Incidence of acute hepatitis C, by sex — United States, 2000–2013

Source: National Notifiable Diseases Surveillance System (NNDSS)

Figure 4.4. Incidence of acute hepatitis C, by race/ethnicity — United States, 2000–2013

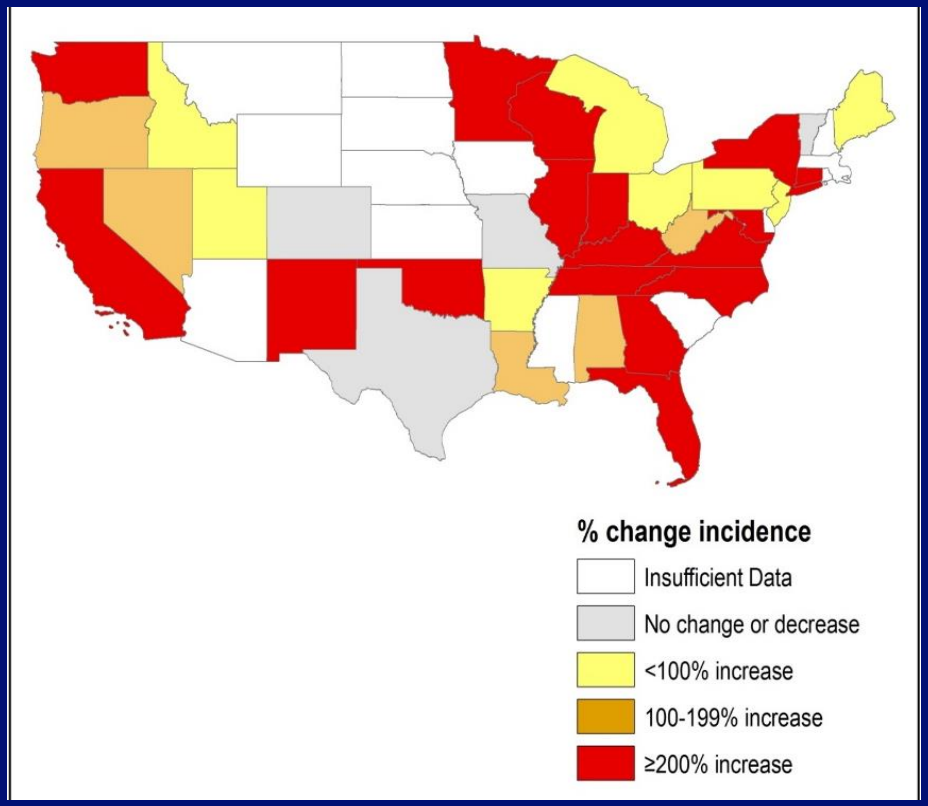


Source: National Notifiable Diseases Surveillance System (NNDSS)

Change in HCV Incidence by State and by County: 2006 Versus 2012

Of the 34 states that reported to CDC in both 2006 and 2012:

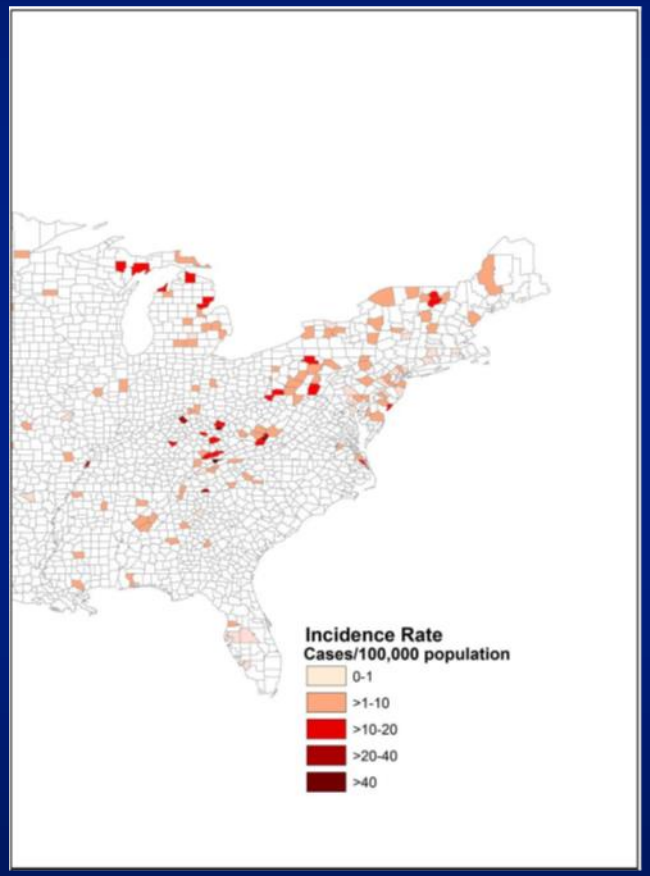
- **30 states reported increases**
- **15 states reported >200% increase**
- **50% of cases were younger than 30 years**



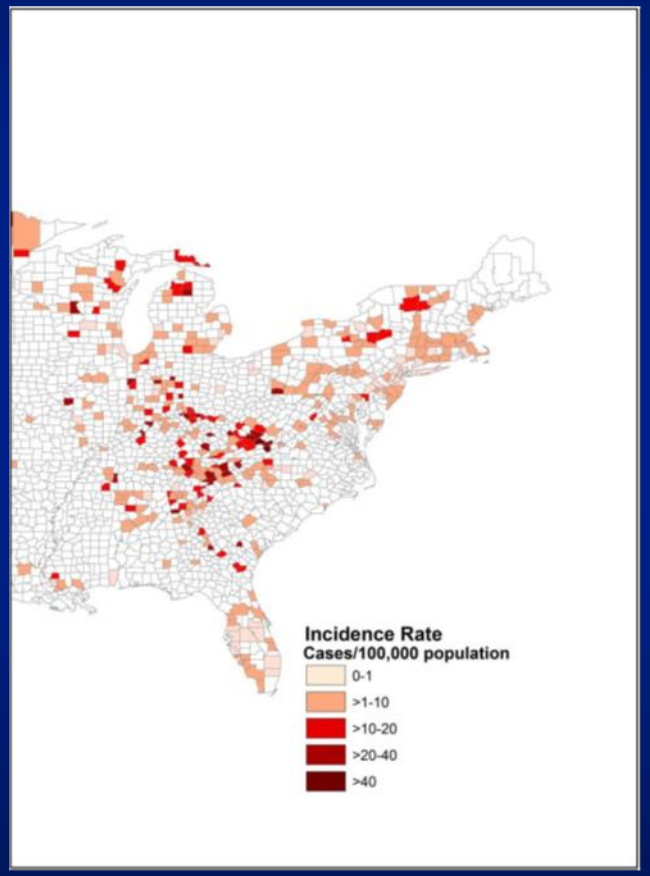
From: Suryaprasad et al, *Clin Infect Dis*: 2014; 59 (15 Nov):1411-19

Greatest HCV increase seen in non-urban—especially, rural and Appalachian counties-- east of the Mississippi

2006



2012



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From: Suryaprasad et al, *Clin Infect D*is 2014; 59:1411-9

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Trends observed in Massachusetts, Wisconsin, Michigan, and Ohio ('ELC Studies')

- These PWIDs were mainly:
  - young (aged 20-29 yrs);
  - white; roughly equal gender distribution
  - non-urban (suburban, rural); and
  - previous oral prescription opioid users ('Oxycontin'/ oxycodone) users, who transitioned to injecting heroin

Drugs used and age of initiation, interviews in 6 jurisdictions, 2011-2012*

Drug	N	%	Mean age started
Marijuana	413	91%	14.1 years old
Alcohol	379	83%	15.2 years old
Powder Cocaine	324	71%	17.4 years old
Any prescription opioid drugs	345	76%	17.7 years old
'Oxycontin' or oxycodone	337	74%	17.9 years old
Methamphetamines	134	29%	18.7 years old
Crack cocaine	245	54%	18.8 years old
Methadone	161	35%	19.3 years old
Heroin	280	61%	19.7 years old

From: Suryaprasad et al, *Clin Infect Dis*: 2014; 59 (15 Nov):1411-19

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These cases reported to CDC represent the "tip of the iceberg"

- Our recent best calculation is that each acute HCV case reported to CDC represents at least 13.2 actual cases*

- Thus, we estimate about 30,000 new HCV infections each year currently (mostly in those < 30 yo)

* RM Klevens et al *Am J Public Health* 2014 Mar; 104(3):48

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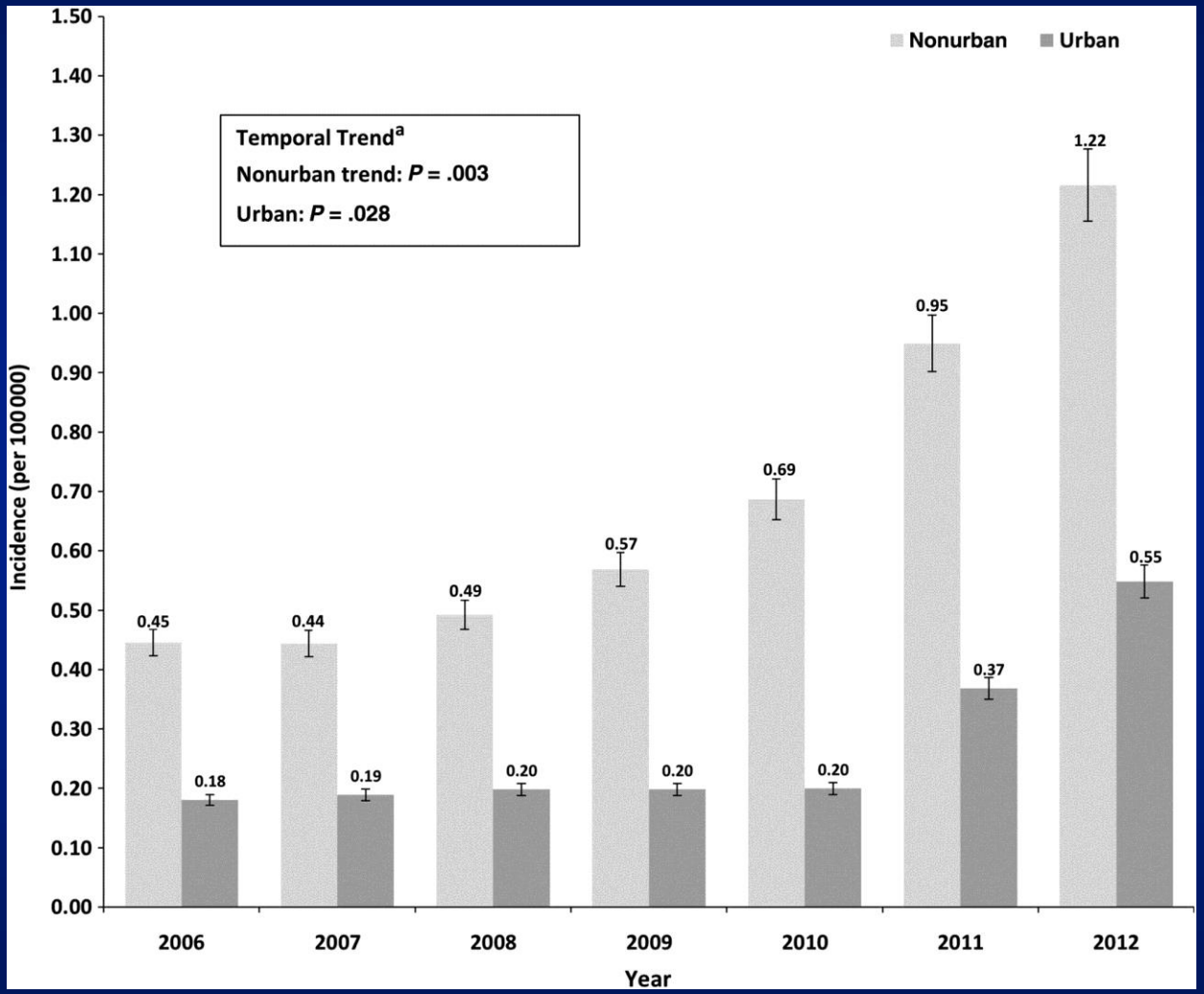
Trends in incidence of acute hepatitis C among young persons reported to CDC, by urbanicity, 2006–2012.



From: AG Suryaprasad et al. *Clin Infect Dis* 2014;59:1411-19

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The Non-urban Outbreak is Occurring in Tandem with Ongoing Urban Outbreaks

Acute HCV Cases *Reported* to CDC in 2013*

State	No. Cases (rate†)
Kentucky	226 (5.1)
Indiana	175 (2.7)
Massachusetts	174 (0.9)
Florida	134 (0.7)
New York	131 (0.7)
Ohio	116 (1.0)
New Jersey	106 (1.2)
Tennessee	98 (1.5)
Pennsylvania	81 (0.6)
North Carolina	79 (0.8)
Michigan	74 (0.7)

* From: DVH Surveillance Summary 2013
† per 100,000 population

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The Epidemiologic "W's" as we understand them:

- Who: young, usually under 30 yo, often under 24 yo; mainly white, non-minority, roughly equal gender distribution
- What: Injection of heroin or dissolved oral prescription opioids
- Where: Biggest increase in rural and suburban areas, esp east of the Mississippi. However, also some increase seen in urban areas

Next “W”: What’s next?

Future work needs to move forward with focus on how to:

- Get all identified PWIDs to opioid substitution treatment (OST) centers or to needle/syringe exchange programs (NSEPs);
- Get all HCV-infected PWIDs linked to care for their HCV and other infections

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There are many barriers to addressing the largest infectious disease epidemic in the United States

- *Clinician attitudes*: this is a 'benign' chronic condition
- *Patient issues*: many barriers, including personal
- *Public attitudes*: "AIDS Fatigue" (*add*: Ebola, SARS, pandemic flu, etc). Also, reluctance to help injection drug users
- *Political attitudes:* No strong advocacy: most HCV patients are PWIDs formerly

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Summary

- Hepatitis C is the largest, if unappreciated, infectious disease epidemic in the United States
- Deaths in chronic HCV-infected persons far outstrip deaths from HIV and 60 other infectious conditions reportable to CDC
- We are in the midst of an “emerging” epidemic of acute HCV in young non-urban persons who transition from prescription oral opioids to injectable heroin, often in their teens
- Control of the ‘chronic’ and the ‘acute’ outbreaks will require a multipronged approach along a testing-to-cure continuum of care

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Thank you

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